



Expres Mail No. EV335610765US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: Orest W. Blaschuk et al.
Group Art Unit: 1631
Application No: 10/006,869
Filed: December 3, 2001
For: COMPOUNDS AND METHODS FOR MODULATING
NONCLASSICAL CADHERIN-MEDIATED FUNCTIONS
Examiner: Marjorie A. Moran
Docket No.: 100086.407C7

DECLARATION OF OREST W. BLASCHUK, Ph.D.

Commissioner for Patents
Washington, D.C. 20231

The undersigned, Dr. Orest Blaschuk, hereby declares:

1. I am the Chief Scientist and co-founder of Adherex Technologies Incorporated, the assignee of the subject application. I am also an Associate Professor in both the Department of Urology and the Department of Anatomy and Cell Biology at McGill University. I have co-authored over 50 scientific publications in peer-reviewed journals and am a named inventor on over 20 issued U.S. Patents, the vast majority of these publications and patents relating to the area of cell adhesion molecules. My *Curriculum Vitae* along with a list of publications and patents is provided as Attachment A. The following experiments were carried out under my direction.

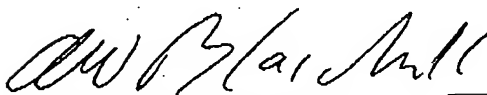
2. In a first experiment, human umbilical vein endothelial cells (HUVEC) were obtained from Cambrex Bio Science Walkersville Inc. (Walkersville, MD). HUVEC were cultured in endothelial growth media (EGM-2) supplemented with 2% FBS, hEGF, hydrocortizone, Gentamicin, Amphotericin-B, VEGF, hFGF-B, R³-IGF-1, ascorbic acid and

heparin. The cells were kept in a humidified atmosphere (5% CO₂) at 37°C. All culture reagents were purchased from Cambrex Bio Science Walkersville Inc. (Walkersville, MD). Cells were exposed to cyclic peptides ADH142 (Ac-CDAEC-OH) or ADH191 (Ac-CDAEC-NH₂) at 1 mg / ml. for 24 hr, and then fixed with 4% paraformaldehyde, followed by 3 washes with phosphate buffered saline (PBS) and staining with hematoxylin. Cells were viewed under light microscopy at 400x. The cyclic peptides ADH142 and ADH191 caused a perturbation of cell-cell contacts in the monolayer. The cells retracted from one another, and became spindle shaped with long processes. Large holes became apparent in the monolayer indicating a disruption of cell-cell adhesion (Figures 1 and 2).

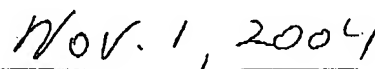
3. In another experiment, dermal human adult microvascular endothelial cells (HMVEC-d) cells were obtained from Cambrex Bio Science Walkersville Inc. (Walkersville, MD). HMVEC-d were cultured in endothelial cell media (EGM-2MV) supplemented with 5% FBS, hEGF, hydrocortizone, Gentamicin, Amphotericin-B, VEGF, hFGF-B, R³-IGF-1 and ascorbic acid. The cells were kept in a humidified atmosphere (5% CO₂) at 37°C. All culture reagents were purchased from Cambrex Bio Science Walkersville Inc. (Walkersville, MD). Cells were exposed to cyclic peptides ADH142 (Ac-CDAEC-OH) or ADH191 (Ac-CDAEC-NH₂) at 1 mg / ml. for 24 hr, and then fixed with 4% paraformaldehyde, followed by 3 washes with phosphate buffered saline (PBS) and staining with hematoxylin. Cells were viewed under light microscopy at 400x. The cyclic peptides ADH142 and ADH191 caused a perturbation of cell-cell contacts in the monolayer. The cells retracted from one another and large holes became apparent in the monolayer indicating a disruption of cell-cell adhesion (Figures 3 and 4).

Application No. 10/006,869

4. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful, false statements, and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.



Orest W. Blaschuk, Ph.D.



Date



Express Mail No. EV335610765US

CURRICULUM VITAE

Date of Last Revision: July 6, 2004

A. IDENTIFICATION

Name: Orest William Blaschuk

Office Address: Urology Research Laboratories, Room H6.15
Royal Victoria Hospital
687 Pine Avenue West
Montreal, Quebec H3A 1A1

Home Address: Apartment 1520
4998 De Maisonneuve West
Westmount, Quebec H3Z 1N2

Telephone: 514-489-9340

FAX: 514-489-5242

Mobile phone: 514-838-5236

E-mail: Orest.Blaschuk@mcgill.ca

Date of Birth: October 20, 1954

Citizenship: Canadian

Place of Birth: Winnipeg, Manitoba, Canada

B. EDUCATION

University of Winnipeg	Winnipeg, Manitoba	B.Sc.	1975	Chemistry
University of Manitoba	Winnipeg, Manitoba	M.Sc.	1979	Biochemistry
University of Toronto	Toronto, Ontario	Ph.D.	1984	Biochemistry

TITLE OF MASTER THESIS: Studies on Glycosidases in Concanavalin A-Sensitive and Resistant Chinese Hamster Ovary Cells Grown in Tissue Culture (May, 1979), University of Manitoba, Winnipeg.

Supervisor: Dr. J.C. Jamieson

TITLE OF DOCTORAL THESIS: Purification and Characterization of a Cell Aggregating Factor (Clusterin) from Ram Rete Testis Fluid (June, 1984), University of Toronto, Toronto.

Supervisor: Dr. I.B. Fritz

Post-Doctoral Research Training:

July, 1984-1986, Department of Biology, Princeton University, Supervisor: Dr. M.S. Steinberg

C. APPOINTMENTS

Current Positions:

Chief Scientist and Co-founder
Adherex Technologies Incorporated
Ottawa, Ontario
Appointed September 18, 1998
Adherex is listed on the Toronto Stock Exchange (Symbol AHX). The IPO was on June 5, 2001.

Associate Professor
Division of Urology
Department of Surgery
McGill University
Appointed June 1, 1993
(unpaid leave of absence taken April 1, 1999 – March 31, 2000)

Associate Professor
Department of Anatomy & Cell Biology
McGill University
Appointed June 1, 1993

Former Positions:

Chief Scientist and Co-founder
Adherex Incorporated
Westmount, Quebec
Appointed September 3, 1996 – April 30, 2001
(Adherex Inc. was amalgamated with Adherex Technologies Inc. on April 30, 2001)

Assistant Professor
 Division of Urology
 Department of Surgery
 McGill University
 Appointed January 1, 1987 - May 31, 1993

Assistant Professor
 Department of Anatomy
 McGill University
 Appointed January 1, 1990 - May 31, 1993

D. SPECIAL HONORS, AWARDS, RECOGNITION

Schools Science Fair Entrance Scholarship	U. of Winnipeg	1972-1973
Chemistry Department Scholarship	U. of Winnipeg	1973-1974
Winnipeg RH Institute Proficiency Scholarship	U. of Winnipeg	1973-1974
University of Manitoba Fellowship	U. of Manitoba	1978-1979
Canadian Medical Research Council Studentship	U. of Toronto	1981-1984
Canadian Medical Research Council Fellowship	Princeton U.	1985-1986
Best Basic Science Paper Award	Canadian Fertility and Andrology Society	1989
Best Basic Science Poster Award	Canadian Fertility and Andrology Society	1993
Listed in <i>American Men & Women of Science</i>		1994
Murray L. Barr Junior Scientist Award	Canadian Association of Anatomists	1995
Applied Research Award	Ottawa Life Sciences Council	2000

E. RESEARCH

1. Research Activities

I am engaged in studies concerning the structure, function and regulation of a family of cell adhesion molecules, known as the cadherins.

F. PUBLICATIONS (*Indicates a member of my laboratory group)

a. Articles in peer-reviewed journals:

- i. **Blaschuk, O.W., J.C. Jamieson and J.A. Wright.** 1980. Studies on hexosaminidase forms in Chinese hamster ovary cells. *Enzyme* 25: 161-169.

- ii. **Blaschuk, O.W., J.C. Jamieson and J.A. Wright.** 1980. Changes in glycosidase activities in concanavalin A-resistant and sensitive mammalian cells. *Int. J. Biochem.* 12: 635-638.
- iii. **Blaschuk, O.W., J.C. Jamieson and J.A. Wright.** 1980. Studies on the hexosaminidases from concanavalin A-resistant and sensitive cell lines. A model system for the study of secretion and uptake of lysosomal enzymes. *Exp. Cell Res.* 130: 451-455.
- iv. **Blaschuk, O.W., J.C. Jamieson and J.C. Eales.** 1982. Properties of hexosaminidases in cell-free extracts of rainbow trout livers and effects of thyroid hormones. *Comp. Biochem. Physiol.* 73B: 729-734.
- v. Fritz, I.B., K. Burdzy, B. Setchell and **O.W. Blaschuk.** 1983. Ram rete testis fluid contains a protein (clusterin) which influences cell-cell interactions *in vitro*. *Biol. Reprod.* 28: 1173-1188.
- vi. **Blaschuk, O.W., K. Burdzy and I.B. Fritz.** 1983. Purification and characterization of a cell-aggregating factor (clusterin), the major glycoprotein in ram rete testis fluid. *J. Biol. Chem.* 258: 7714-7720.
- vii. **Blaschuk, O.W. and I.B. Fritz.** 1984. Isoelectric forms of clusterin isolated from ram rete testis fluid and from secretions of primary cultures of ram and rat Sertoli cell-enriched preparations. *Can. J. Biochem. Cell Biol.* 62: 456-461.
- viii. **Blaschuk, O.W., R.L. Manteuffel and M.S. Steinberg.** 1986. Purification of desmoglein 2. A method for the preparation and fractionation of desmosomal components. *Biochem. Biophys. Acta* 883: 426-431.
- ix. **Blaschuk, O.W. and R. Farookhi.** 1989. Estradiol stimulates cadherin expression in rat granulosa cells. *Develop. Biol.* 136: 564-567.
- x. **Blaschuk, O.W., Y. Pouliot and P.C. Holland.** 1990. Identification of a conserved region common to cadherins and influenza strain A hemagglutinins. *J. Mol. Biol.* 211: 679-682.
- xi. **Blaschuk, O.W., R. Sullivan, S. David and Y. Pouliot.** 1990. Identification of a cadherin cell adhesion recognition sequence. *Develop. Biol.* 139: 227-229.
- xii. Pouliot, Y., P.C. Holland and **O.W. Blaschuk.** 1990. Developmental regulation of a cadherin during the differentiation of skeletal myoblasts. *Develop. Biol.* 141: 292-298.
- xiii. Chuah, M.I., S. David and **O.W. Blaschuk.** 1991. Differentiation and survival of olfactory epithelial neurons in dissociated cell culture. *Develop. Brain Rés.* 60: 123-132.
- xiv. *Chen, B., **O.W. Blaschuk** and B.F. Hales. 1991. Cadherin mRNAs during rat embryo development *in vivo* and *in vitro*. *Teratology* 44: 581-590.
- xv. Coutifaris, C., L.-C. Kao, H.M. Sehdev, U. Chin, G.O. Babalola, **O.W. Blaschuk** and J.F. Strauss, III. 1991. E-cadherin expression during the differentiation of human trophoblasts. *Development* 113: 767-777.

- xvi. *Cyr, D.G., L. Hermo, **O.W. Blaschuk** and B. Robaire. 1992. Distribution and regulation of epithelial cadherin messenger ribonucleic acid and immunocytochemical localization of epithelial cadherin in the rat epididymis. *Endocrinology* 130: 353-363.
- xvii. *Cyr, D.G., **O.W. Blaschuk** and B. Robaire. 1992. Identification and developmental regulation of cadherin messenger ribonucleic acids in the rat testis. *Endocrinology* 131: 139-145.
- xviii. Byers, S., E. Amaya, *S. Munro and **O.W. Blaschuk**. 1992. Fibroblast growth factor receptors contain a conserved HAV region common to cadherins and influenza strain A hemagglutinins: A role in protein-protein interactions? *Develop. Biol.* 152: 411-414.
- xix. *MacCalman, C.D., *N. Bardeesy, P.C. Holland and **O.W. Blaschuk**. 1992. Noncoordinate developmental regulation of N-cadherin, N-CAM, integrin, and fibronectin mRNA levels during myoblast terminal differentiation. *Develop. Dynamics* 195: 127-132.
- xx. Newton, S.C., **O.W. Blaschuk** and C.F. Millette. 1993. N-cadherin mediates Sertoli cell- spermatogenic cell adhesion. *Develop. Dynamics* 197: 1-13.
- xxi. Alexander, J.S., **O.W. Blaschuk** and F.R. Haselton. 1993. An N-cadherin-like protein contributes to solute barrier maintenance in cultured endothelium. *J. Cell Physiol.* 156: 610-618.
- xxii. *MacCalman, C.D., D.A. O'Brien, S.W. Byers and **O.W. Blaschuk**. 1993. N-cadherin expression in the seminiferous epithelium of the mouse testis. *Endocrine J.* 1: 519-525.
- xxiii. Byers, S.W., S. Sujarit, B. Jegou, S. Butz, H. Hoschutzky, K. Herrenknecht, *C. MacCalman and **O.W. Blaschuk**. 1994. Cadherins and cadherin associated molecules in the developing and maturing rat testis. *Endocrinology* 134: 630-639.
- xxiv. *MacCalman, C.D. and **O.W. Blaschuk**. 1994. Gonadal steroids regulate N-cadherin mRNA levels in the mouse testis. *Endocrine* 2 : 157-163.
- xxv. *MacCalman, C.D., P. Brodt, *J.D. Doublet, *R. Jednak, M.M. Elhilali, M. Bazinet and **O.W. Blaschuk**. 1994. The loss of E-cadherin mRNA transcripts in rat prostatic tumors is accompanied by increased expression of mRNA transcripts encoding fibronectin and its receptor. *Clin. Exp. Metastasis* 12: 101-107.
- xxvi. *MacCalman, C.D., R. Farookhi and **O.W. Blaschuk**. 1994. Estradiol and progesterone regulate E-cadherin mRNA levels in the mouse uterus. *Endocrine* 2: 485-490.
- xxvii. *MacCalman, C.D., R. Farookhi and **O.W. Blaschuk**. 1994. Estradiol regulates E-cadherin mRNA levels in the surface epithelium of the mouse ovary. *Clin. Exp. Metastasis* 12: 276-282.
- xxviii. *MacCalman, C.D., R. Farookhi and **O.W. Blaschuk**. 1995. Estradiol regulates N-cadherin mRNA levels in the mouse ovary. *Developmental Genetics* 16: 20-24.

- xxix. *Munro, S.B., *I.M. Turner, R. Farookhi, **O.W. Blaschuk** and S. Jothy. 1995. E-cadherin and OB-cadherin mRNA levels in normal human colon and colon carcinoma. *Exp. Molec. Pathology* 62: 118-122.
- xxx. *Munro, S.B., A.J. Duclos, *A.R. Jackson, M.G. Baines and **O.W. Blaschuk**. 1996. Characterization of cadherins expressed by murine thymocytes. *Cell. Immunology* 169: 309-312.
- xxxi. Kerkette K, **O.W. Blaschuk** and R. Farookhi. 1996. Cellular heterogeneity in the membrana granulosa of developing rat follicles: assessment by flow cytometry and lectin binding. *Endocrinology* 137: 3089-3100.
- xxxii. *Munro, S.B. and **O.W. Blaschuk**. 1996. A comprehensive survey of the cadherins expressed in the testes of fetal, immature, and adult mice using the polymerase chain reaction. *Biol. Reprod.* 55: 822-827.
- xxxiii. Farookhi, R., *C.-S. Geng, *C.D. MacCalman and **O.W. Blaschuk**. 1997. Hormonal regulation of N-cadherin mRNA levels in rat granulosa cells. *Annals N.Y. Acad. Sci.* 816: 165-172.
- xxxiv. *MacCalman, C.D., *S. Getsios, R. Farookhi and **O.W. Blaschuk**. 1997. Estrogens potentiate the stimulatory effects of follicle-stimulating hormone on N-cadherin messenger ribonucleic acid levels in cultured mouse Sertoli cells. *Endocrinology* 138: 41-48.
- xxxv. Getsios, S., G.T.C. Chen, M.D. Stephenson, *P. LeClerc, **O.W. Blaschuk** and C.D. MacCalman. 1998. Regulated expression of cadherin-6 and cadherin-11 in the glandular epithelial and stromal cells of the human endometrium. *Developmental Dynamics* 211: 238-247.
- xxxvi. Alexander, J.S., T. Dayton, C. Davis, S. Hill, T.H. Jackson IV, **O. Blaschuk**, *M. Symonds, N. Okayama, C.G. Kevil and S.M. Berney. 1998. Activated T-lymphocytes express occludin, a component of tight junctions. *Inflammation* 22: 573-582.
- xxxvii. Woodward, T.L., M.A. Sia, **O.W. Blaschuk**, J.D. Turner and D.W. Laird. 1998. Fibroblast-epithelial cell heterocellular gap junctional communication is mediated by an intermediate cell type but not by E-cadherin transgene expression. *J. Cell Sci.* 111: 3529-3539.
- xxxviii. Ibrahim, N.M., M.H.T. Troedsson, D.N. Foster, K.J. Loseth, J.A. Farris, **O. Blaschuk** and B.G. Crabo. 1999. Reproductive tract secretions and bull spermatozoa contain different clusterin isoforms that cluster cells and inhibit complement-induced cytotoxicity. *J. Andrology* 20: 230-240.
- xxxix. Makrigiannakis, A., G. Coukos, M. Christofidou-Soiomidou, B.J. Gour, G.L. Radice, **O. Blaschuk** and C. Coutifaris. 1999. N-cadherin mediated human granulosa cell adhesion prevents apoptosis: A role in follicular atresia and luteolysis? *Am. J. Pathol.* 154: 1391-1406.
- xl. Wilby, M.J., E.M. Muir, J. Fok-Seang, B.J. Gour, **O.W. Blaschuk** and J. Fawcett. 1999. N-cadherin inhibits Schwann cell migration on astrocytes. *Mol. Cell. Neurosci.* 14: 66-84.
- xli. Makrigiannakis, A., G. Coukos, **O. Blaschuk** and C. Coutifaris. 2000. Follicular atresia and luteolysis: Evidence of a role for N-cadherin. *Annals N.Y. Acad. Sci.* 900: 46-55.

- xlii. Schnädelbach, O., **O.W. Blaschuk**, *M. Symonds, B.J. Gour, P. Doherty and J.W. Fawcett. 2000. N-cadherin influences migration of oligodendrocytes on astrocyte monolayers. *Mol. Cell. Neurosci.* 15: 288-302.
- xlili. Williams, E., G. Williams, B.J. Gour, **O.W. Blaschuk** and P. Doherty. 2000. A novel family of cyclic peptide antagonists suggest that N-Cadherin specificity is determined by amino acids that flank the HAV motif. *J. Biol. Chem.* 275: 4007-4012.
- xliv. Williams, E., G. Williams, B.J. Gour, **O. Blaschuk** and P. Doherty. 2000. INP, a novel antagonist and candidate specificity determining motif for N-cadherin. *Mol. Cell. Neurosci.* 15: 456-464.
- xlv. Machell, N.H., **O.W. Blaschuk** and R. Farookhi. 2000. Developmental expression and distribution of N- and E-cadherin in the rat ovary. *Biol. Reprod.* 63: 797-804.
- xlvi. Schnädelbach, O., I. Ozen, **O.W. Blaschuk**, B.J. Gour, R.L. Meyer and J.W. Fawcett. 2001. N-cadherin is involved in axon-oligodendrocyte contact and myelination. *Mol. Cell. Neurosci.* 17: 1084-1093.
- xlvii. Fadel, M.P., M. Szewczenko-Pawlikowski, *P. Leclerc, E. Dziak, *J.M. Symonds, **O. Blaschuk**, M. Michalak and M. Opas. 2001. Calreticulin affects {beta}-catenin associated pathways. *J. Biol. Chem.* 276: 27083-27089.
- xlvi. Machell, N.H., **O.W. Blaschuk**, and R. Farookhi. 2002. Expression and localization of P-, K-, and OB-cadherin in the prepubertal rat ovary. *Mol. Reprod. Dev.* 61: 142-54.
- xlix. **Blaschuk, O.W.**, T. Oshima, B.J. Gour, *M. Symonds, J.H. Park, C.G. Kevil, S.D. Trocha, S. Michaud, N. Okayama, J.W. Elrod and J.S. Alexander. 2002. Identification of an occludin cell adhesion recognition sequence. *Inflammation* 26: 193-198.
- l. Feltes, C.M., A. Kudo, **O. Blaschuk** and S.W. Byers. 2002. An alternatively spliced cadherin-11 enhances human breast cancer cell invasion. *Cancer Res.* 62: 6688-6697.
- li. Oshima, T., **O. Blaschuk**, B. Gour,* M. Symonds, J.W. Elrod, M. Sasaki, T.H. Jackson and J.S. Alexander. 2003. Tight junction peptide antagonists enhance neutrophil trans-endothelial chemotaxis. *Life Sciences* 73: 1729-1740.
- lii. Erez, N., E. Zamir, B.J. Gour, **O.W. Blaschuk** and B. Geiger. 2004. Induction of apoptosis in cultured endothelial cells by a cadherin antagonist peptide: involvement of fibroblast growth factor receptor-mediated signalling. *Exp. Cell Res.* 294: 366-78.
- b. Reviews and Book Chapters
 - i. Fritz, I.B., **O.W. Blaschuk** and K. Burdzy. 1985. Properties of clusterin, a glycoprotein which elicits cell aggregation, and immunochemical determination of levels in ovine tissues. In: Symposium on Gonadal Proteins and Peptides (M.R. Sairam and L.E. Atkinson, eds.). pp. 311-325. World Scientific Publishing Co., Philadelphia.

- ii. Steinberg, M.S., H. Shida, G.J. Giudice, M. Shida, N.H. Patel and **O.W. Blaschuk**. 1987. On the Molecular Organization, Diversity and Functions of Desmosomal Proteins. In: Junctional Complexes of Epithelial Cells (S. Clark, ed.). Ciba Found. Symp. 125: 3-25. John Wiley and Sons Ltd., London.
- iii. Farookhi, R. and **O.W. Blaschuk**. 1989. E-cadherin May be Involved in Mediating FSH-Stimulated Responses in Rat Granulosa Cells. In: Growth Factors and the Ovary (A.N. Hirshfield, ed.). pp. 257-266. Plenum Press, New York.
- iv. Farookhi, R. and **O.W. Blaschuk**. 1991. Cadherins and Ovarian Follicular Development. In: Signalling Mechanisms and Gene Expression in the Ovary (G. Gibori, ed.). pp. 254-260. Springer-Verlag, New York, NY.
- v. Byers, S.W. and **O.W. Blaschuk**. 1992. Epithelial Barriers, Cell-Cell Adhesion and Mucosal Immunity in Male Reproductive Tract Tissues. In: Local Immunity in Reproductive Tract Tissues. pp. 147-159. Cambridge University Press.
- vi. Byers, S.W., B. Jegou, *C.D. MacCalman and **O.W. Blaschuk**. 1993. Sertoli Cell Adhesion Molecules and the Collective Organization of the Testis. In: The Sertoli Cell (L.D. Russell and M. Griswold, eds.). pp. 461-476. Cache River Press, Clearwater Fl.
- vii. **Blaschuk, O.W.**, *S.B. Munro and R. Farookhi. 1994. E-cadherin, estrogens, and cancer: Is there a connection? The Can. J. Oncology 4: 291-301.
- viii. **Blaschuk, O.W.**, *S.B. Munro and R. Farookhi. 1995. Cadherins, steroids and cancer. Endocrine 3: 83-89.
- ix. Jothy, S., *S.B. Munro, L. LeDuy, D. McClure and **O.W. Blaschuk**. 1995. Adhesion or anti-adhesion in cancer: what matters more? Cancer Metastasis Rev. 14: 363-376.
- x. *Munro, S.B. and **O.W. Blaschuk**. 1996. The Structure, Function, and Regulation of Cadherins. In: Tumor Cell Adhesion and Cancer Invasion (P. Brodt, ed.). pp. 17-34. R.G. Landes Company, Austin TX.
- xi. *Rowlands, T.M., *J.M. Symonds, R. Farookhi and **O.W. Blaschuk**. 2000. Cadherins: Crucial regulators of structure and function in reproductive tissues. Reviews in Reproduction. 5: 53-61.
- xii. *Rowlands, T.M. and **O.W. Blaschuk**. 2000. Function and regulation of cadherins in reproductive tissues. Recent Res. Devel. Endocrinol. 1: 273-305.
- xiii. **Blaschuk, O.W.** and *T.M. Rowlands. 2000. Cadherins as modulators of angiogenesis and the structural integrity of blood vessels. Cancer Metastasis Rev. 19: 1-5.
- xiv. **Blaschuk, O.W.** and *T.M. Rowlands. 2002. Plasma membrane components of adherens junctions. Mol. Membr. Biol. 19: 75-80.

- xv. **Blaschuk, O.W.** and J.M. Symonds. 2003. Synthetic Antiangiogenic Agents. In: Burger's Medicinal Chemistry and Drug Discovery, Sixth Edition, Volume 5: Chemotherapeutic Agents (D.J. Abraham, ed.). pp. 215-222. John Wiley & Sons, Inc., New York NY.

c. Patents:

- i. Title: Compounds and methods for modulating cell adhesion.
Inventors: **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,031,072
Date of Patent: February 29, 2000
- ii. Title: Compounds and methods for modulating tissue permeability.
Inventors: **Orest W. Blaschuk**, J. Matthew Symonds and Barbara J. Gour
United States Patent Number: 6,110,747
Date of Patent: August 29, 2000
- iii. Title: Compounds and methods for modulating cell adhesion.
Inventors: **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,169,071
Date of Patent: January 2, 2001
- iv. Title: Compounds and methods for regulating cell adhesion.
Inventors: **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,203,788
Date of Patent: March 20, 2001
- v. Title: Compounds and methods for modulating neurite outgrowth
Inventors: **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,207,639
Date of Patent: March 27, 2001
- vi. Title: Compounds and methods for modulating tissue permeability
Inventors: **Orest W. Blaschuk**, J. Matthew Symonds and Barbara J. Gour
United States Patent Number: 6,248,864
Date of Patent: June 19, 2001
- vii. Title: Compounds and methods for modulating adhesion molecule function
Inventors: Patrick Doherty, **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,277,824
Date of Patent: August 21, 2001
- viii. Title: Compounds and methods for modulating beta-catenin

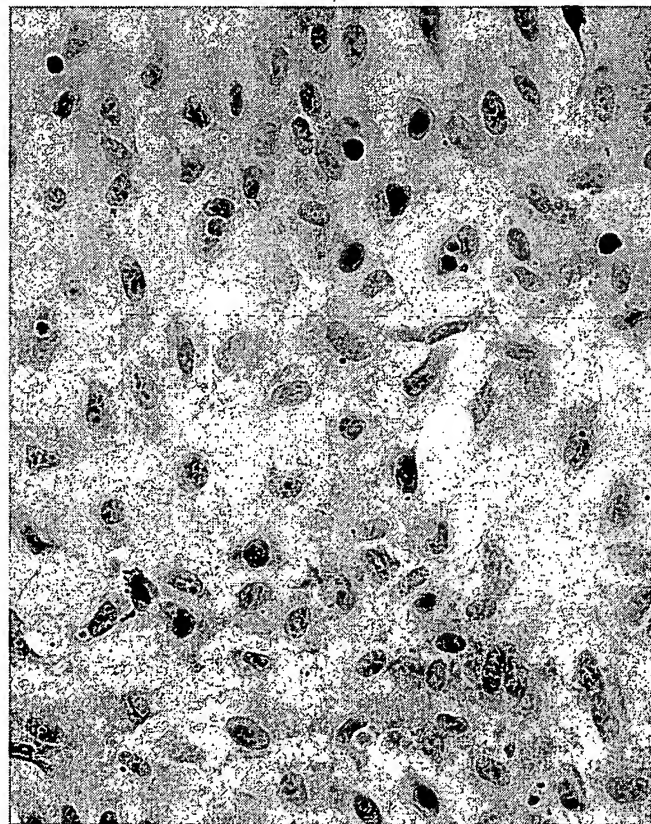
	Inventors:	mediated gene expression Orest W. Blaschuk , Stephen Byers and Barbara J. Gour
	United States Patent Number:	6,303,576
	Date of Patent:	October 16, 2001
ix.	Title:	Compounds and methods for modulating tissue permeability
	Inventors:	Orest W. Blaschuk , James Matthew Symonds and Barbara J. Gour
	United States Patent Number:	6,310,177
	Date of Patent:	October 30, 2001
x.	Title:	Compounds and methods for modulating cell adhesion
	Inventors:	Orest W. Blaschuk and Barbara J. Gour
	United States Patent Number:	6,326,352
	Date of Patent:	December 4, 2001
xi.	Title:	Compounds and methods for modulating neurite outgrowth
	Inventors:	Orest W. Blaschuk and Barbara J. Gour
	United States Patent Number:	6,333,307
	Date of Patent:	December 25, 2001
xii.	Title:	Compounds and methods for modulating cell adhesion
	Inventors:	Orest W. Blaschuk and Barbara J. Gour
	United States Patent Number:	6,346,512
	Date of Patent:	February 12, 2002
xiii.	Title:	Compounds and methods for modulating nonclassical cadherin-mediated functions
	Inventors:	Orest W. Blaschuk and Barbara J. Gour
	United States Patent Number:	6,358,920
	Date of Patent:	March 19, 2002
xiv.	Title:	Compounds and methods for modulating junctional adhesion molecule-mediated functions
	Inventors:	Orest W. Blaschuk , James Matthew Symonds and Barbara J. Gour
	United States Patent Number:	6,391,855
	Date of Patent:	May 21, 2002
xv.	Title:	Compounds and methods for cancer therapy
	Inventors:	Orest W. Blaschuk , Barbara J. Gour and Riaz Farookhi
	United States Patent Number:	6,417,325
	Date of Patent:	July 9, 2002
xvi.	Title:	Compounds and methods for inhibiting cancer metastasis
	Inventors:	Orest W. Blaschuk , James Matthew Symonds, Stephen Byers

- and Barbara J. Gour
United States Patent Number: 6,433,149
Date of Patent: August 13, 2002
- xvii. Title: Compounds and methods for cancer therapy
Inventors: **Orest W. Blaschuk**, Barbara J. Gour, Riaz Farookhi and Anmar Ali
United States Patent Number: 6,465,427
Date of Patent: October 15, 2002
- xviii. Title: Compounds and methods for modulating OB-cadherin mediated cell adhesion
Inventors: **Orest W. Blaschuk**, James Matthew Symonds and Barbara J. Gour
United States Patent Number: 6,472,367
Date of Patent: October 29, 2002
- xix. Title: Compounds and methods for modulating adhesion molecule function
Inventors: Patrick Doherty, **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,472,368
Date of Patent: October 29, 2002
- xx. Title: Compounds and methods for inhibiting the interaction between .alpha.-catenin and .beta.-catenin
Inventors: **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,551,994
Date of Patent: April 22, 2003
- xxi. Title: Compounds and methods for modulating apoptosis
Inventors: **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,562,786
Date of Patent: May 13, 2003
- xxii. Title: Antibody that specifically binds to the cadherin-5 cell adhesion recognition sequence
Inventors: **Orest W. Blaschuk**, James Matthew Symonds and Barbara J. Gour
United States Patent Number: 6,569,996
Date of Patent: May 27, 2003
- xxiii. Title: Compounds and methods for inhibiting cancer metastasis
Inventors: **Orest W. Blaschuk**, James Matthew Symonds, Stephen Byers and Barbara J. Gour
United States Patent Number: 6,593,297
Date of Patent: July 15, 2003

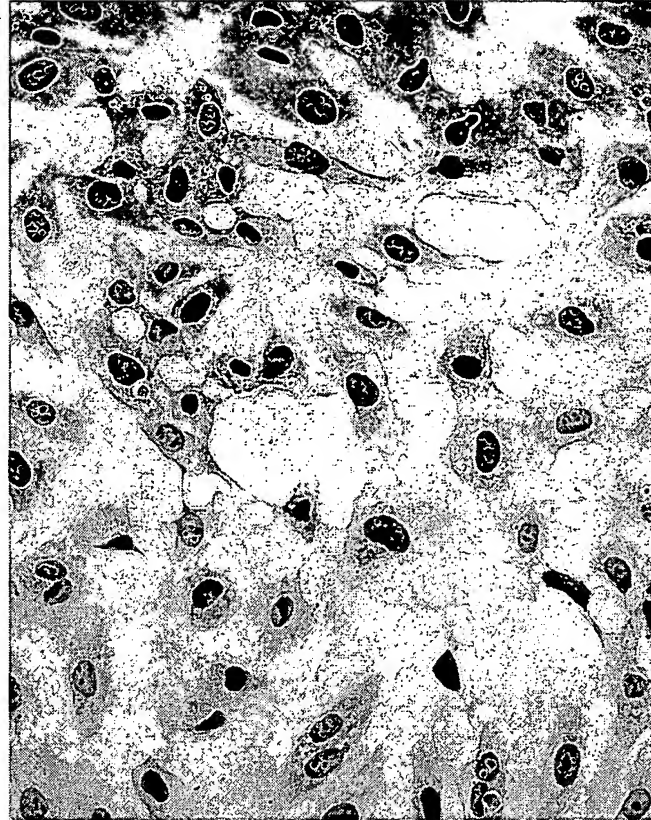
- xxiv. Title: Compounds and methods for modulating endothelial cell adhesion
Inventors: **Orest W. Blaschuk**, Barbara J. Gour, Riaz Farookhi and Anmar Ali
United States Patent Number: 6,610,821
Date of Patent: August 26, 2003
- xxv. Title: Compounds and methods for modulating desmosomal cadherin-mediated functions
Inventors: **Orest W. Blaschuk**, James Matthew Symonds and Barbara J. Gour
United States Patent Number: 6,638,911
Date of Patent: October 28, 2003
- xxvi. Title: Methods for treating cancer by modulating .beta.-catenin mediated gene expression
Inventors: **Orest W. Blaschuk**, Stephen Byers and Barbara J. Gour
United States Patent Number: 6,677,116
Date of Patent: January 13, 2004
- xxvii. Title: Methods for diagnosing and evaluating cancer
Inventors: **Orest W. Blaschuk**, James Matthew Symonds, Stephen Byers and Barbara J. Gour
United States Patent Number: 6,680,175
Date of Patent: January 20, 2004
- xxviii. Title: Methods for diagnosing and evaluating cancer
Inventors: **Orest W. Blaschuk**, James Matthew Symonds, Stephen Byers and Barbara J. Gour
United States Patent Number: 6,682,901
Date of Patent: January 27, 2004
- xxix. Title: Compounds and methods for stimulating gene expression and cellular differentiation
Inventors: **Orest W. Blaschuk** and Barbara J. Gour
United States Patent Number: 6,683,048
Date of Patent: January 27, 2004
- xxx. Title: Compounds and methods for stimulating .beta.-catenin mediated gene expression and differentiation
Inventors: **Orest W. Blaschuk**, Stephen Byers and Barbara J. Gour
United States Patent Number: 6,706,685
Date of Patent: March 16, 2004
- xxxi. Title: Compounds and methods for modulating claudin-mediated

		functions
	Inventors:	Orest W. Blaschuk , James Matthew Symonds and Barbara J. Gour
	United States Patent Number:	6,723,700
	Date of Patent:	April 20, 2004
xxxii.	Title:	Compounds and methods for modulating claudin-mediated functions
	Inventors:	Orest W. Blaschuk , James Matthew Symonds and Barbara J. Gour
	United States Patent Number:	6,756,356
	Date of Patent:	June 29, 2004

Figure 1: Disruption of human umbilical vein endothelial cell (HUVEC) monolayers by treatment with cyclic peptide ADH142 (Ac-CDAEC-OH 1 mg / mL medium) for 24 hr



Control (medium only) 400x



ADH142 1mg/ml 400x

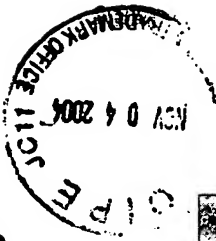
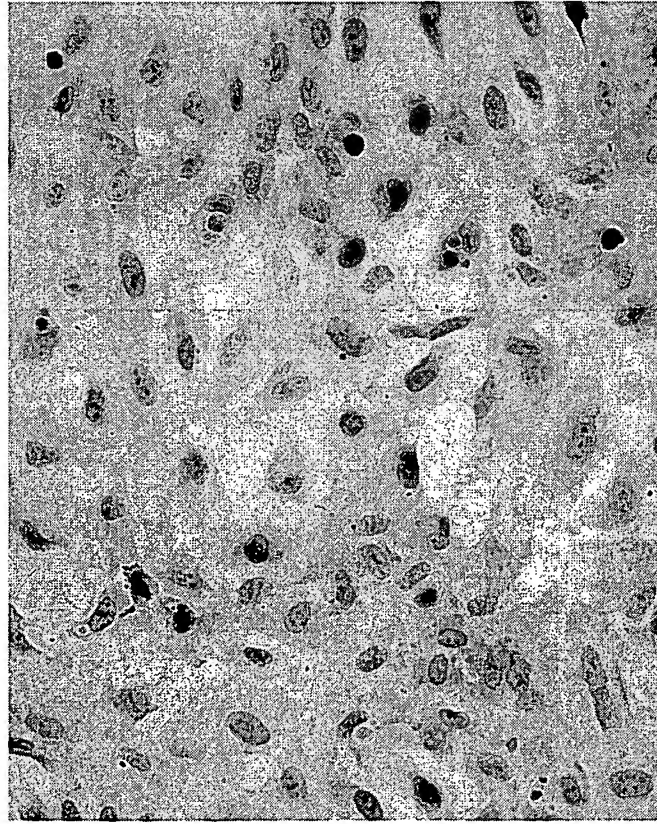
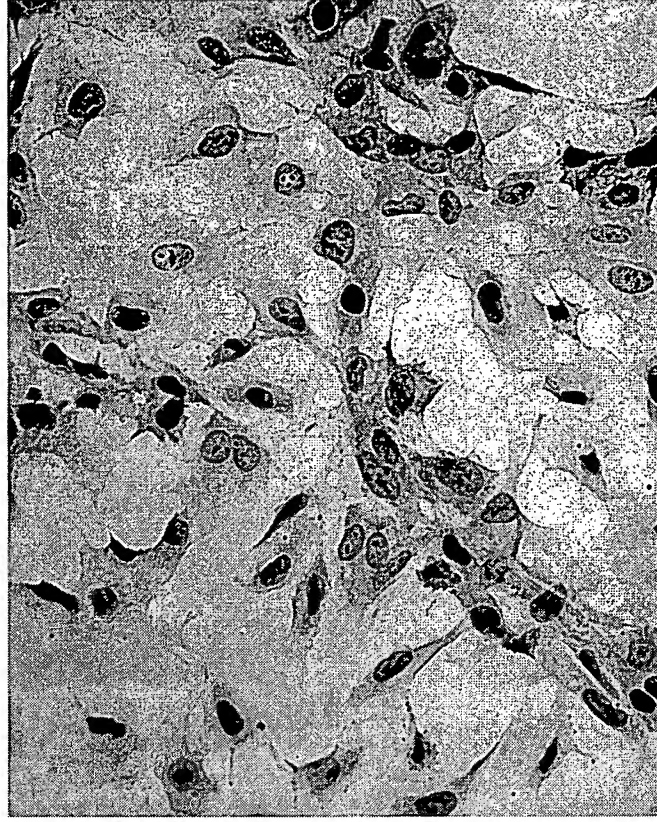


Figure 2: Disruption of human umbilical vein endothelial cell (HUVEC) monolayers by treatment with cyclic peptide ADH191 (Ac-CDAEC-NH2 1 mg / mL medium) for 24 hr

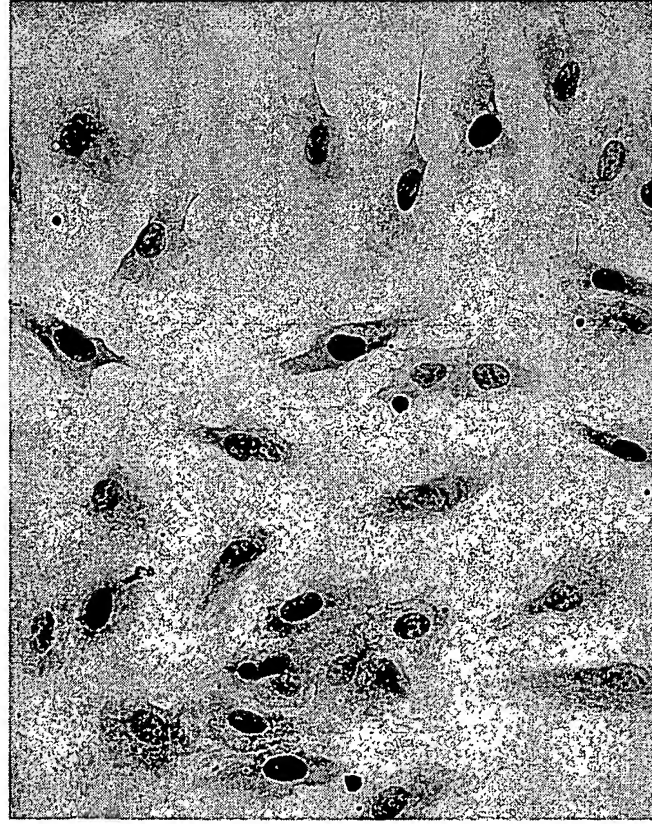


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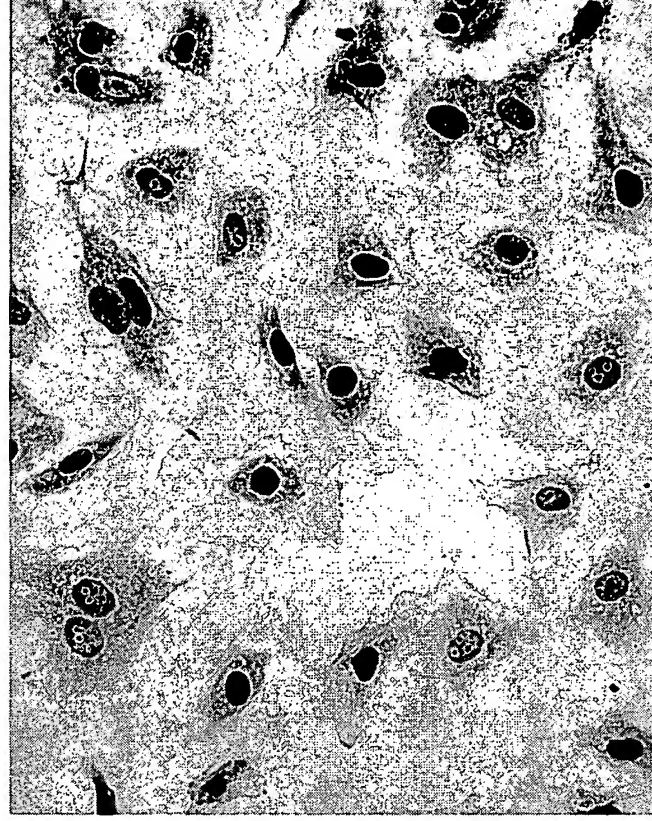


ADH191 1mg/ml 400x

Figure 3: Disruption of human microvessel endothelial cell (HMVEC) monolayers by treatment with cyclic peptide ADH142 (Ac-CDAEC-OH) (1 mg / mL medium) for 24 hr

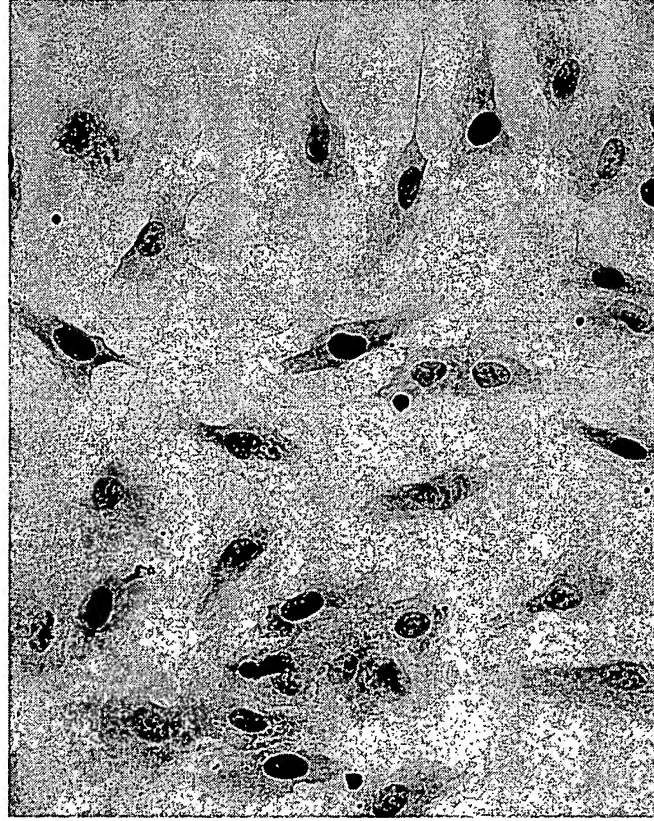


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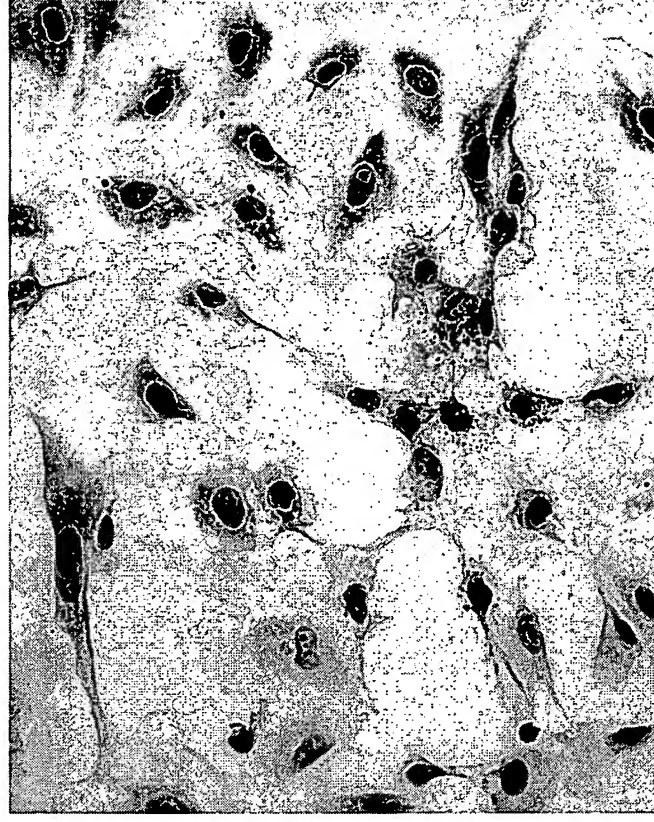


ADH142 1mg/ml 400x

Figure 4: Disruption of human microvessel endothelial cell (HMVEC) monolayers by treatment with cyclic peptide ADH191 (Ac-CDAEC-NH₂) (1 mg / mL medium) for 24 hr



Control (medium only) 400x



ADH191 1mg/ml 400x